

REMARKS

This submission is in response to the Office Action dated November 28, 2007. Claims 58, 60, 62-71, 89, 91-94 and 96-125 are currently rejected. Reconsideration of the above-identified application, in view of the following remarks, is respectfully requested. Each of the Examiner's rejections is discussed below.

Telephone Examiner Interview

Applicants thank Examiner Kendra Carter and Supervising Examiner Sreenivasan Padmanabhan for discussing this application on January 16, 2008. The obviousness rejections, particularly the motivation to combine Morlet and Fox and the statement of synergy in Fox were discussed. The potential future actions, including providing information regarding synergy, appeal, and requesting a pre-appeal conference, were discussed.

First Rejection under 35 U.S.C. §103

Claims 58, 60, 62-64, 68-71, 89, 92, 93, 96, 98-103, 105-106, 108-114, and 117-124 have been rejected as obvious over WO 97/00076 to Morlet in view of Fox (U.S. Pat. 5,374,432) and further in view of Smith (U.S. Pat. 5,576,006). The Examiner states that Morlet and Fox teach the desirability of providing a topical antimicrobial compositions having a biguanides polymer and antimicrobial metal as claimed and further, that Fox teaches that a combination of silver with other antimicrobials provides improved antimicrobial efficacy.

Applicants respectfully traverse. The Examiner states that Morlet, Smith, and Fox each teach antimicrobial compositions and thus are proper to combine. The mere fact that references can be combined or modified in one of many particular ways does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination, *see* MPEP 2143.01. The art does not provide either the suggestion or desirability to combine the references in such a way to arrive at the present invention. A person of ordinary skill in the art would not select such a combination as claimed in the present invention without some particular teaching or reasoning to do so. To combine these references and then to arrive at the present invention, a person of ordinary skill in the art would have to pick and choose among a large number of different compounds or compositions to form a composition having: an organic polycationic polymer such as a biguanide polymer, an antimicrobial metallic material (material is substantially water-insoluble or can be rendered substantially water-insoluble) and (a) a

carrier selected from the group consisting of a cream, a lotion, a deodorant, a spray, a gel, a wax, an oil, an ointment, a soap, and an alcohol, and/or (b) a skin-compatible component selected from the group consisting of emollients, thickeners, humectants, skin moisturizing agents, and surfactants, and/or (c) a formulation which is a dermal antiseptic formulation, and/or (d) a composition which can be administered by spreading or immersion. This composition particularly forms a moisture-resistant film on the skin, which imparts a persistent antimicrobial activity on the skin. Further, as discussed below, these references do not teach or suggest each element of the claimed invention. Thus, applicants respectfully request that this rejection be withdrawn.

In particular, the Examiner states that Fox teaches improved antimicrobial efficacy for a combination of antimicrobials (col. 1 lines 25 – 33 and col. 2 lines 30-45) and Fox thus provides a motivation to combine two antimicrobials and further, in response to Applicant's arguments, that the Fox reference should be taken as a whole, and that the "variety of antibiotics that the Fox reference refers to is therefore any antibiotic which is found suitable for use in topical ocular applications."

Applicants respectfully traverse this rejection. While the Fox reference should be considered for what it teaches and also for what it fairly suggests (*In re Baird*, 16 F.3d 380 (Fed. Cir. 1994)), a person of ordinary skill in the art would look to the whole of the art in the field, not just to Fox when determining what the art teaches and suggests. Other references disclose that combining antimicrobials do not provide a synergistic effect, and provide nothing more than a simple combination. For example:

A. Kuruvilla JR, Kamath MP, *J Endod.* 1998 Jul; 24(7):472-6. This abstract discloses the combination of sodium hypochlorite and chlorhexidine gluconate for use as an endodontic irrigant. The reduction of bacterial cultures with the combination was compared to with the two antimicrobials alone and it was found that the difference in reduction of bacterial cultures was not significant compared to the use of chlorhexidine gluconate alone.

B. White RR, Janer LR, Hays GL., *Am J Dent.* 1999 Jun; 12(3):148-50. This abstract disclosed similar results as in Kuruvilla *et al.* There was no significant difference between the use of chlorhexidine gluconate alone and combined with sodium hypochlorite.

C. Murthy P, Nilssen EL, Rao S, McClymont L.G., *Clin Otolaryngol Allied Sci.* 1999 Jun;24(3):228-31. The combination of antibiotics as an antiseptic nasal carrier cream was studied for the treatment of epistaxis. Naseptin cream alone was compared with Naseptin cream and silver nitrate cautery. There was no statistically significant difference in outcome between the two treatment groups.

D. Snelling CF, et al., *J Burn Care Rehabil.* 1991 Jan-Feb; 12(1):13-8. Wound bacterial colonization for patients treated with silver sulfadiazine alone and silver sulfadiazine combined with chlorhexidine digluconate was studied for various bacterial cultures. The combination was more effected

for treating colonization by *Staphylococcus aureus*. However, no statistical difference was found for colonization by *Enterococcus faecalis*, *Pseudomonas aeruginosa*, or *Enterobacter cloacae*.

E. Modak SM, Sampath L, Fox CL Jr. *J Burn Care Rehabil.* 1988 Jul-Aug; 9(4):359-63. Treatment of burn wounds with quinolones alone and quinolones combined with silver sulfadiazine was studied. While the ability of *Pseudomonas Aeruginosa* to form resistant mutants was diminished in the combination, the antifungal or antibacterial properties of the individual drugs were not affected by the combination.

(Each Abstract A – E are provided herewith in Exhibit I).

Thus, a person of ordinary skill in the art, looking at the prior art as a whole, would not presume that combining two antimicrobials would have improved antimicrobial efficacy as generically suggested by Fox. Such a person would understand that this is an unpredictable area, and any improvements would have to be determined by trial and error of the particular combinations of interest.

Therefore, person of ordinary skill in the art would have no more reason to combine Fox with Morlet and/or Smith than to combine the teachings of one of Abstracts A – E with Morlet and/or Smith, which would teach against the effectiveness of combining two antimicrobials and thus teaches away from the presently claimed invention.

The Examiner also states that Smith teaches forming complexes of antimicrobial compounds that are less water soluble and the desirability of forming a complex with a more insoluble higher molecular weight molecule, such as polyhexamethylene biguanide hydrochloride. However, Smith does not teach or suggest the aspect of the claimed invention as suggested by the Examiner. Thus, applicants respectfully traverse.

Particularly, independent claims 58, 89, 92, 93, 96, 98, 103, and 105 are each limited to methods including a steps of administering a composition “which is substantially water-insoluble or can be rendered substantially water-insoluble” and “forming a moisture-resistant film on the skin.” Smith, which teaches forming less water soluble compounds, does not teach insoluble compositions. As described in the Declaration by Dr. Samuel Sawan, provided herewith, Smith teaches the use of polycarboxylic acids and functional biocides to reduce the water solubility of such functional biocides through the reaction of the two. However, such compounds would be expected to have significant water solubility since they are prepared in water and form solutions in water. Smith further teaches the use of a polycationic metal salt

with a polycarboxylic acid and a cationic antimicrobial compound, which forms a Coulombic complex. Such complexes between acids and bases will dissociate in aqueous environments releasing significant levels of the antimicrobial compound attached to the polycarboxylic acid. Thus, there is no reason a person of ordinary skill in the art, upon reading Smith, would consider forming a substantially water-insoluble composition as described in the presently claimed invention.

Additionally, neither Morlet nor Fox teach a composition on the skin which is substantially water-insoluble or can be rendered substantially water-insoluble and they further do not teach a film that is moisture resistant and has persistent antimicrobial activity.

Thus, the presently claimed invention provides a composition that, since it is substantially water-insoluble, is moisture-resistant and thereby imparts persistent antimicrobial activity on the skin, is not anticipated or made obvious by Smith, Morlet and/or Fox. A person of ordinary skill in the art would not be motivated to modify Smith, Fox, or Morlet in the manner described in the present invention to obtain the claimed method.

For at least these reasons, claims 58, 89, 92, 93, 96, 98, 103, and 105 and the remainder of the claims which depend therefrom are patentable over Morlet in view of Fox and Smith. Thus, claims 58, 60, 62-64, 68-71, 89, 92, 93, 96, 98-103, 105-106, 108-114, and 117-124 are not obvious over Morlet in view of Fox and/or Smith. Therefore, Applicants therefore request that this rejection be withdrawn.

Second Rejection under 35 U.S.C. §103

Claims 65-67, 91, 94, 97, 104, 107, and 115 – 116 are rejected as obvious over Morlet in view of Fox, Smith, and further in view of WO 95/17152 (the '152 publication). The Examiner contends that Smith teaches forming complexes of antimicrobial compounds that are less water soluble, Fox teaches the combination of silver with other antimicrobials provides improved antimicrobial efficacy, and the combination of Morlet, Smith, and Fox is proper.

The Examiner states that Smith clearly teaches the benefits of the polyhexamethylene biguanide in antimicrobial compositions and Sawan teaches providing the biguanide in derivatized form as well as the use of silver iodide and thus it would have been obvious to provide the biguanidine adduct as taught by Sawan in the composition of Morlet et al., Fox and Smith, with the expectation of providing a suitable antimicrobial composition. Thus, the burden is shifted to the Applicant to show that the prior art product does not possess or render obvious the same properties as the instantly claimed product.

